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EXAMINER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/486,094	Applicant(s) FREYSSINET ET AL.	
	Examiner Anne Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *11-18 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,19-35 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-10, 19-35 and 39) in Paper No. 12 is acknowledged. The traversal is on the ground(s) that Groups I and IV share a single inventive concept and common technical feature (the nucleic acid for androctonine) and should be examined together. This is not found persuasive because Groups I and IV are drawn to different methods of use of androctonine nucleic acids. Under PCT lack of unity rules, only one method of use of a product is permitted per group. The method of use of group I has different method steps, different starting materials and different effects from the method of use of group IV.

Claims 11-18 and 36-38 are withdrawn from consideration as being drawn to nonelected inventions. Claims 1-10, 19-35 and 39 are examined.

The requirement is still deemed proper and is therefore made FINAL.

Drawings

2. The drawings are objected to for the reasons indicated on the accompanying form PTO 948. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

Specification

3. The disclosure is objected to because the faint lettering could result in printing problems. For that reason, a substitute specification excluding the claims is required pursuant to 37 CFR 1.125(a).

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

Sequence Rules

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from the specification (*e.g.*, pg 3, line 17) and the claims (*e.g.*, claim 4).

The amino acid sequences in SEQ ID NOs:1 and 3 must be listed separately from the nucleic acid sequences. A new paper copy of the sequence listing and a new computer readable form are required. See 37 CFR 1.821 through 1.825.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set for in this Office action will be held to be non-responsive.

Claim Objections

5. Claims 1-10, 19-35 and 39 are objected to because of the following informalities:

Claims 1-10, 19-35 and 39 lack an article at the start of the claim.

There is an article missing before "plant" in claim 28.

In claim 3, line 5, claim 10, line 4, and claim 19, lines 5 and 6, "the said" in should be either "the" or "said".

In claims 9-10, the phrase "the sequence identifier No. 1 (SEQ ID NO:1)" should be replaced with --SEQ ID NO:1--, and in claim 10, line 5, "this" should be deleted.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to nucleic acid fragments, which are products of nature.

The nucleic acid fragments, as claimed, have the same characteristics and utility as those found naturally in the genome or as cellular precursors thereof and therefore do not constitute patentable subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that the claims be modified to refer to the hand of the inventor, *e.g.* by replacing "Nucleic acid fragment" in claim 1 with --An isolated nucleic acid fragment--.

8. Claims 32 and 35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to progeny plants and seeds, which are products of nature.

The progeny plants and seeds encompass nontransformed plants and seeds that have the same characteristics and utility as those found in nature and therefore do not constitute patentable subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that the claims be modified to refer to the hand of the inventor, *e.g.* by indicating that the progeny plants and seeds comprise the chimeric gene.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-10, 19-35 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that encode an androctonine. In contrast, the specification only describes a coding sequence from *Androctonis australis* that comprises SEQ ID NO:1. Applicant does not describe other DNA molecules

encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

The instant specification defines androctonines as peptides produced by scorpions (pg 2, lines 6-7). The instant specification fails to provide a description of structural features of all peptide-encoding nucleic acids from all species of scorpion and of the structural features that distinguish scorpion genes from genes from other organisms.

Additionally, not all nucleic acids encoding the motif of SEQ ID NO:12 are from scorpions (see, *e.g.*, the sequence search results)

Hence, Applicant has not, in fact, described DNA molecules that encode a scorpion peptide or encode the motif of SEQ ID NO:12 within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

See *In re Shokal*, 113 USPQ 283, (CCPA 1957) at pg 285

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189 ; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary. ...
> We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

11. Claims 1-10, 19-35 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding an androctonine of SEQ ID NO:1, a chimeric gene, vector, transformed bacterium and plant comprising the nucleic acid, and method of transformation of tobacco with the nucleic acid, does not reasonably provide enablement for nucleic acids encoding an androctonine of any sequence and plants transformed with those nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a multitude of nucleic acids encoding an androctonine, which is any peptide from scorpion, a method of transforming a multitude of host organisms with those nucleic acids, and host organisms so obtained. The claims are also drawn to nucleic acids

that are "homologous sequences" of the nucleic acid of SEQ ID NO:1 or that encode "homologous peptides" of the protein of SEQ ID NO:1.

The instant specification, however, only provides guidance for a nucleic acid construct encoding the PR-1a signal sequence from tobacco (SEQ ID NO:2) fused to an androctonine coding sequence (SEQ ID NO:1) and plant and *Agrobacterium* transformation vectors comprising the construct (example 1), and transformation of tobacco and testing the transformed tobacco for tolerance to the herbicide bromoxynil (example 2).

The instant specification fails to provide guidance for nucleic acids encoding any peptide from scorpion or for nucleic acids encoding homologues of SEQ ID NO:1. The instant specification also fails to provide guidance for transformation of a yeast, fungus or baculovirus. The specification also fails to provide guidance for producing fungal-resistant plants. Lastly, the specification fails to provide guidance for expression of the protein encoded by SEQ ID NO:1, which has no starting methionine, without attaching a signal peptide.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically

reduced enzyme activity (see Table 1). All these mutated proteins, however, would be "homologous peptides" of the original protein.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding homologues of the protein of SEQ ID NO:1. Making all possible single amino acid substitutions in an 25 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{25} nucleic acids. Because nucleic acids encoding homologues of the protein of SEQ ID NO:1 would have many more than a single substitution, nucleic acids with many more substitutions would need to be made and analyzed.

Expressing pesticidal peptides in plants is also unpredictable. Okamoto et al (1998, Plant Cell Physiol. 39:57-63) transformed tobacco plants with a gene encoding a short antimicrobial peptide behind a constitutive promoter. The peptide was so unstable in plants that it could not be detected, even though the mRNA encoding it was expressed at high levels (pg 59, left column, last paragraph, to pg 60, entire left column). Similarly, Allefs et al (1995, Am. Potato J. 72:437-445) teach that potato plants transformed with a gene encoding the antimicrobial peptide cecropin B degrade the peptide and have no increase in resistance to infection (pg 441-443).

Even when peptides are not degraded in the transgenic plants, they unexpectedly do not retain their biological activity. Peptides that are effective pesticides when isolated and contacted with microorganisms or fed to insects do not function as pesticides when genes encoding them are transformed into plants. When tobacco plants were transformed with a gene encoding cecropin B, the transformed plants displayed no increase in disease resistance (Hightower et al, 1994, Plant Cell Rep. 13:295-299, see pg 297, paragraph spanning the columns, to pg 298, right

column, paragraph 1). De Bolle et al (1996, Plant Mol. Biol. 31:993-1008) teach that tobacco plants transformed with genes encoding seed antimicrobial peptides had no increase in resistance to infection (pg 1004, paragraph spanning the columns). Lastly, Pang et al (1992, Gene 116:165-172) teach that in tobacco plants transformed with a gene encoding the scorpion insectotoxin I_5A, the peptide is not correctly processed and the resulting plants had no paralytic effect on tobacco budworm (pg 170, right column).

As the specification does not describe the production of fungus-resistant plants that have been transformed with a gene encoding an androctonine, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with fungus-resistance, if such plants are even obtainable.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 3-10, 19-35 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. Many of these are listed below.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim

does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 2 recites the broad recitation "the androctonine ... from scorpions", and the claim also recites "in particular from the species *Androctonus australis*" which is the narrower statement of the range/limitation. Similarly, claim 2 recites the broad recitation "at least 20 amino acids" and also recites the narrower limitation "preferably at least 20 amino acids". Claim 10 recites the broad recitation "SEQ ID NO:1" and also recites the narrower limitation "more particularly the coding position of this SEQ ID NO:1". Claim 19 recites the broad recitation "host organism" and also recites the narrower limitation "in particular plant cells or plants". Claims 20, 25 and 29 recite the broad recitations "bacteria", yeasts" and "fungi" and also recite the narrower limitations "for example *E. coli*", "in particular yeast of the genera *Saccharomyces* or *Kluyveromyces, Pichia*", and "in particular *Aspergillus*". Claim 23 recites the broad recitation "host organisms" and also recites the narrower limitation "in particular plant cells". Claim 28 recites the broad recitation "host organisms" and also recites the narrower limitation "plant cell or plant". Claim 34 recites the broad recitation "fungal diseases"

and also recites the narrower limitation "such as those caused by ...." with numerous even narrower limitations.

Claim 3 is indefinite in its recitations of "4 cysteine residues which form disulphide bridges between themselves". A cysteine cannot form a disulfide bond with itself. If Applicant intended that the bonds be formed among the residues, the claim should be so amended.

Claim 4 is indefinite in its recitation of "essentially comprises". It is unclear how great a deviation from the sequence Applicant intended.

Claim 6 lacks antecedent basis for the limitation "the basic amino acids" in line 2. Additionally, asparagine and homoasparagine are not basic amino acids.

Claims 6, 20, 25, 29 and 33 are not written in proper Markush format. The claims should be in the format "selected from the group consisting of A, B, C and D." The phrase "chosen from" should be replaced with -- selected from the group consisting of--. In claims 20, 25 and 29 all group members should be singular. See MPEP § 2173.05(h).

Claim 9 is indefinite in its recitation of "homologous peptide sequences". The definition of "homologous" on page 8, lines 21-25, of the specification applies only to nucleic acid sequences.

Claim 9 lacks antecedent basis for the limitation "the homologous peptide sequences."

In claim 19, "these elements being" should be replaced with --wherein these elements are--.

In claim 19, it is unclear if the phrase "as defined according to claim 1" is intended to modify "androctonine" or "DNA fragment".

Claims 20, 25 and 29 are indefinite in reciting "baculovirus" as an organism as viruses are not recognized as organisms. Additionally, it not clear how it can be transformed.

Claim 21 lacks antecedent basis for the limitation "the transformed host organism."

Claim 21 is indefinite in its recitation of "adapted to the transformed host organism". The manner in which the selection marker is adapted is unclear. Additionally, it is not clear what is intended by the phrase "selection marker". Does Applicant mean a gene encoding a selectable marker?

Claims 23-27 and 39 are indefinite because the steps involved in the methods/processes do not start with a verb in the gerund form.

In claim 23, it is unclear into what the nucleic acid fragment is incorporated.

Claim 23 lacks antecedent basis for "nucleic acid fragment ... of claim 19" as claim 19 is drawn to a chimeric gene. An alternative interpretation of that claim is that the nucleic acid fragment has no relationship to the chimeric gene of claim 19, and that the process is one of transforming host organisms with any nucleic acid.

It is unclear in claim 24 if the chimeric gene is on the vector or if the chimeric gene is incorporated by means of a co-transformation method.

Claim 25 lacks antecedent basis for the limitation "the host organism" in line 2.

It is unclear in the method of claim 27 how plants can be regenerated from transformed plant cells when in the method of claim 25 only one plant cell was transformed.

Claim 30 lacks antecedent basis for the limitation "transformed plant cells according to claim 29" as claim 29 is drawn to host organisms.

Claims 31-34 lack antecedent basis for the limitation "Plant".

Claim 32 lacks antecedent basis for the limitation "the regenerated plants according to claim 31."

Claim 35 lacks antecedent basis for the limitation "Plant seeds".

Claims 39 lacks antecedent basis for the limitation "the transformed host organism" in line 3.

Claim 39 is indefinite in its recitation of "an appropriate cultivation environment" as this environment is not defined.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1-10, 19-25, 28-29 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Maeda et al (1991, Virol. 184:777-780).

Maeda et al teach a chimeric gene encoding a scorpion toxin AaIT, which would be an androctonine, that "essentially comprises" SEQ ID NO:12 from amino acids 10-27 (Figure 1). This stretch has a lysine. The region "essentially comprises" the amino acids indicated in claims 7-8 of the instant application. AaIT would be a "homologous peptide sequence" of the amino acid sequence in SEQ ID NO:1 and the nucleic acid would be an homologous sequence of the nucleic acid sequence in SEQ ID NO:1. The chimeric gene functions in a baculovirus and is in an expression vector with a selection marker that is "adapted" to the host organism. Maeda et al

also teach host organisms (*B. mori* cells) transformed with the vector via a baculovirus (pg 777, right column, paragraph 2). Lastly, Maeda et al teach a method of purifying the protein from the transformed host organism (pg 778-779).

16. Claims 1-10, 19-32, 34 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Ely (WO 95/11305).

Ely teaches a chimeric gene encoding the scorpion toxin AaHIT, which would be an androctonine, that "essentially comprises" SEQ ID NO:12 from amino acids 10-27 (see SEQ ID NO:1). This stretch has a lysine. The region "essentially comprises" the amino acids indicated in claims 7-8 of the instant application. AaHIT would be an "homologous peptide sequence" of the amino acid sequence in SEQ ID NO:1 and the nucleic acid would be a homologous sequence of the nucleic acid sequence in SEQ ID NO:1. The chimeric gene functions in a baculovirus and is in an expression vector with a selection marker that is "adapted" to the host organism. Ely also teaches plants transformed with the vector (pg 9, paragraphs 1 and 4, and claim 7). The plants would be resistant to at least some fungal diseases because a pathogenic fungus cannot infect all plants. Lastly, Ely teaches a method of purifying the protein from the transformed host organism (paragraph spanning pg 7-8).

17. Claims 1-10 and 19-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Barton et al (1993, US Patent 5,177,308).

Barton et al teach a chimeric gene encoding the scorpion toxin AaIT, which would be an androctonine, that "essentially comprises" SEQ ID NO:12 from amino acids 11-28 (see Fig 3). This stretch has a lysine. The region "essentially comprises" the amino acids indicated in claims 7-8 of the instant application. AaIT would be an "homologous peptide sequence" of the amino

acid sequence in SEQ ID NO:1 and the nucleic acid would be an homologous sequence of the nucleic acid sequence in SEQ ID NO:1. The chimeric gene functions in plants and bacteria and is in an expression vector with a selection marker that is "adapted" to the host organisms (column 9, lines 1-59). Barton et al also teach tobacco plants transformed with the vector (column 9, lines 44-59, and claims 1-2) and cultivation and crossing of the transformed plants (column 10, lines 37-52). Tobacco is resistant to at least some fungal diseases because a pathogenic fungus cannot infect all plants.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. Claims 1-10, 19-35 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barton et al (*supra*) in view of Sutton et al (1992, Transgen. Res. 1:228-236).

The claims are drawn to a chimeric gene encoding an androctonine that "essentially comprises" SEQ ID NO:12 or is an "homologous peptide sequence" of the amino acid sequence in SEQ ID NO:1, wherein the chimeric gene functions in plants and bacteria and is in an expression vector with a selection marker that is "adapted" to the host organisms. The claims are also drawn to plants transformed with the vector and to cultivation and crossing of the transformed plants, wherein the plants are resistant to at least some fungal diseases.

The teachings of Barton et al are discussed above. Barton et al do not disclose methods of isolating androctonine from host organisms transformed with a nucleic acid encoding that protein.

Sutton et al teach the partial purification of expressed proteins from plants (pg 233).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to isolate proteins, as described in Sutton et al, from the transgenic plants described by Barton et al. One of ordinary skill in the art would have been motivated to do so because analysis of protein expression levels is a standard procedure when expressing proteins in plants,

20. Claims 1-10, 19-35 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ely (*supra*) in view of Gordon-Kamm et al (1990, Plant cell 2:603-618).

The claims are drawn to a chimeric gene encoding an androctonine that "essentially comprises" SEQ ID NO:12 or is an "homologous peptide sequence" of the amino acid sequence in SEQ ID NO:1, wherein the chimeric gene functions in plants and bacteria and is in an expression vector with a selection marker that is "adapted" to the host organisms. The claims are also drawn to plants transformed with the vector and to cultivation and crossing of the transformed plants, wherein the plants are resistant to at least some fungal diseases and wherein the plants include maize.

The teachings of Ely are discussed above. Ely does not disclose maize plants transformed with the chimeric gene and seeds from those plants.

Gordon-Kamm et al teach transformation of maize and production of seeds from the transgenic plants (pg 607-610).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing androctonine-expressing plants as taught by Ely, to transform an androctonine gene into maize as described in Gordon-Kamm et al. One of ordinary skill in the art would have been motivated to do so because of the economic importance of maize.

Conclusion

21. No claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Kimberly Davis, at (703) 305-3015.

Anne R. Kubelik, Ph.D.
April 15, 2002

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